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# NATIONAL PBM BULLETIN

APRIL 18, 2016

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DEPARTMENT OF VETERANS AFFAIRS  
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),  
VISN PHARMACIST EXECUTIVES (VPEs), AND THE CENTER FOR MEDICAL SAFETY (VA MedSAFE)

## METFORMIN: FDA RELAXES WARNINGS FOR USE IN CERTAIN PATIENTS WITH MILD TO MODERATE RENAL INSUFFICIENCY

### I. ISSUE

FDA revises warnings concerning metformin use in certain patients with renal impairment and suggests using a new measurement for determining kidney function. Metformin previously carried a contraindication for renal disease or renal dysfunction (e.g., as suggested by serum creatinine levels  $\geq 1.5\text{mg/dL}$  [males],  $\geq 1.4\text{mg/dL}$  [females]) or abnormal creatinine clearance which may also result from conditions such as cardiovascular collapse (shock), acute myocardial infarction, and septicemia. However, these creatinine levels may have resulted in discontinuing metformin when it could be safely continued with patient benefit. Public reports have urged the FDA to use glomerular filtration rate rather than creatinine clearance, and to allow use in patients with mild-moderate decreases in renal function.

### II. BACKGROUND

Metformin is an antihyperglycemic agent used in the treatment of type 2 diabetes. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Renal tubular secretion is the major route of metformin elimination, and the risk of metformin accumulation and lactic acidosis increases with renal impairment (currently based on serum creatinine levels).

### III. DISCUSSION

FDA recently reviewed evidence in the published medical literature and concluded that metformin may be safely used in patients with mild to moderate renal impairment. New labeling changes will reflect this information. Label revisions will also recommend determining kidney function using glomerular filtration rate (instead of blood creatinine clearance) since it incorporates patient's age, gender, race, and/or weight.

### IV. PROVIDER CONSIDERATIONS/RECOMMENDATIONS

New recommendations from the FDA now allow metformin use in mild-mod renal insufficiency, making many more patients candidates for metformin treatment. FDA recommendations include:

- *Before starting metformin, obtain the patient's eGFR.*
- *Metformin is contraindicated in patients with an eGFR below 30 mL/minute/1.73 m<sup>2</sup>.*
- *Starting metformin in patients with an eGFR between 30-45 mL/minute/1.73 m<sup>2</sup> is not recommended.*
- *Obtain an eGFR at least annually in all patients taking metformin. In patients at increased risk for the development of renal impairment such as the elderly, renal function should be assessed more frequently.*
- *In patients taking metformin whose eGFR later falls below 45 mL/minute/1.73 m<sup>2</sup>, assess the benefits and risks of continuing treatment. Discontinue metformin if the patient's eGFR later falls below 30 mL/minute/1.73 m<sup>2</sup>.*
- *Discontinue metformin at the time of or before an iodinated contrast imaging procedure in patients with an eGFR between 30 and 60 mL/minute/1.73 m<sup>2</sup>; in patients with a history of liver disease, alcoholism, or heart failure; or in patients who will be administered intra-arterial*



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*iodinated contrast. Re-evaluate eGFR 48 hours after the imaging procedure; restart metformin if renal function is stable.*

Providers should continue to report any adverse reactions with the use of metformin products by entering the information into CPRS' Allergies/ Adverse Reactions field and/or via local reporting mechanisms. Adverse events should also be reported, as appropriate, to the VA ADERS program and FDA MedWatch (1-800-FDA-1088, fax 1-800-FDA-0178, online at <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>, or by mail).

### V. REFERENCES

1. FDA Drug Safety Communication: FDA revises warnings regarding use of the diabetes medicine metformin in certain patients with reduced kidney function. <http://www.fda.gov/Drugs/DrugSafety/ucm493244.htm> . (Accessed April 8, 2016)

### ACTIONS

- **Facility Director** (or physician designee): Forward this document to the Facility Chief of Staff (COS).
- **Facility COS and Chief Nurse Executives:** Forward this document to all appropriate providers and health care staff (e.g., **primary care providers, endocrinologists, radiologists, including contract providers, etc.**). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.
- **ACOS for R&D:** Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).